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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,096	02/19/2004	Nadine Carozzi	APA014US01	5854

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

NOTIFICATION DATE	DELIVERY MODE
05/16/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/782,096	CAROZZI ET AL.	
	Examiner	Art Unit	
	ANNE KUBELIK	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *07 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,19,22,23 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,19,22-23 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09/18/2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11, 19, 22-23 and 27 are pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1 and 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dov et al (1996, Appl. Environ. Microbiol., 62:3140-3145) in view of Liu et al (2000, US Patent 6,156,308) and further in view of Carlton et al (1985, Mol. Biol. Microb. Differ., Proc. Intl. Spore Conf., 9th, Meeting date 1984, pages 246-252; Ed. Hoch et al, Am.Soc. Microbiol., Washington, DC) and further in view of deMaagd et al (2001, Trends. Genet. 17:193-199) and taken with the evidence of Applicant's response to the Request for Information under 37 CFR 1.105.

The rejection is repeated for the reasons of record as set forth in the Office action mailed 6 December 2010. Applicant's arguments filed 7 March 2011 have been fully considered but they are not persuasive. Applicant addressed both rejections together; these arguments and their rebuttal are presented after the presentation of the rejections.

Applicant's response to the Request for Information under 37 CFR 1.105, filed 17 March 2009, indicate that the bacterial strain from which SEQ ID NO:1-6 were isolated is HD536, and available from the USDA.

The claims are drawn to a nucleic acid encoding a toxin comprising SEQ ID NO:2, 4 or 6.

Ben-Dov et al teach restriction mapping of a *Bacillus thuringiensis* plasmid (pg 3141, left column, to pg 3143, right column, 3). The method involved isolating the plasmid DNA (pg 3140, right column, ¶4), cloning fragments in vectors that encode a selectable-marker protein heterologous to the endotoxin, and growing these clones were grown in an E. coli host cell (pg 3140, right column, ¶2; pg 3143, right column, ¶2); using the fragments in restriction mapping (pg 3141, left column, to pg 3143, right column, 3). Ben-Dov et al do not teach a nucleic acid encoding SEQ ID NO:2, 4 or 6.

Liu et al teach that it would be advantageous to isolate new *B. thuringiensis* toxins to increase the spectrum of biopesticides (column 3, lines 6-8). Liu et al also teach a method of isolating *B. thuringiensis* toxin genes, involving sequencing the proteins from the toxin crystals, using them to make probes, using the probes to isolate the genes encoding the toxins, and sequencing the genes (column 15, line 19, to column 17, line 25). Liu et al also teach expressing the toxins in heterologous bacteria (column 6, line 25, to column 7, line 31).

Carlton et al teach that strain HD536 has a 68 MDa plasmid implicated in toxin production (Table 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to clone delta-endotoxin genes from strain HD536 described in Carlton et al using the methods described in Ben-Dov et al and Liu et al. One of ordinary skill in the art would have sequenced the plasmid fragments, translate the resulting sequences to identify open reading frames; comparison to known Cry protein conserved sequence and structural domains, as taught by deMaagd et al (paragraph spanning pg 193-194; Fig. 2) would aid indentifying Cry encoding

reading frames. Further, use of probes made by the method Liu et al and designed from the protein sequences of toxins made by HD536 would have aided in cloning toxin genes, including those encoding SEQ ID NO:2, 4 or 6, from that strain. The level of ordinary skill in this art is very high, as evidenced by each of Ben-Dov et al, Liu et al, and deMaagd et al.

One of ordinary skill in the art would have been motivated to do this cloning because an increased repertoire of delta-endotoxins would be desirable for increasing toxicity spectra, as taught by Liu et al (column 3, lines 6-8), and for overcoming pest resistance to existing endotoxins.

It is obvious to use the 68 MDa plasmid from HD536 because HD536 was known in the art as having a toxin-encoding plasmid (Carlton et al, Table 1). In cloning the toxins from the 68 MDa plasmid from HD536 one of skill in the art would necessarily isolate a nucleic acid encoding SEQ ID NO:2, 4 or 6.

It would be obvious to one of skill in the art to culture the host cell comprising the plasmid in conditions under which the nucleic acid encoding the toxins is expressed to study the toxicity of the protein, particularly for toxicity to lepidopteran plant pests, and to produce large quantities of the toxin, as suggested by Liu et al (column 6, lines 25-36).

4. Claims 2-3, 8-11, 19, 22-23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dov et al in view of Liu et al and further in view of Carlton et al and further in view of deMaagd et al as applied to claims 1 and 4-7 above, and further in view of Koziel et al (1997, US Patent 5,625,136).

The rejection is repeated for the reasons of record as set forth in the Office action mailed 6 December 2010, as applied to claims 2-3, 8-11, 19 and 22-23. Applicant's arguments filed 7 March 2011 have been fully considered but they are not persuasive. Applicant addressed both rejections together; these arguments and their rebuttal are presented after the presentation of the rejections.

The claims are drawn to plants transformed with a nucleic acid encoding a toxin comprising SEQ ID NO:2, 4 or 6, including plant optimized nucleic acids.

The teachings of Ben-Dov et al in view of Liu et al and further in view of Carlton et al and further in view of deMaagd et al are discussed above. Ben-Dov et al in view of Liu et al and further in view of Carlton et al and further in view of deMaagd et al do not teach plants and seeds transformed with the nucleic acid.

The teachings of Ben-Dov et al in view of Liu et al and further in view of Carlton et al and further in view of deMaagd et al are discussed above. Ben-Dov et al in view of Liu et al and further in view of Carlton et al and further in view of deMaagd et al do not teach plants and seeds transformed with the nucleic acid.

Koziel et al teach construction of a Cry endotoxin coding sequence that is designed for expression in a plant; this sequence has increased GC content relative to the native coding sequence (column 7, lines 19-56; column 9, lines 50-56). Koziel et al also teach expression of the modified Cry endotoxin coding sequence in maize cells from a vector that also encodes phosphoenolpyrivate carboxylase (column 59, line 40, to column 63, line 50), as well as maize plants and seeds transformed with the modified Cry endotoxin coding sequence (claims 4-25).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to operably link the nucleic acid made obvious by Ben-Dov et al in view of Liu et al and further in view of Carlton et al and further in view of deMaagd et al to a plant promoter and transform the resulting construct into plants, including maize, as described in Koziel et al . One of ordinary skill in the art would have been motivated to do so because the resultant plants will be more resistant to insect pests, and the farmer thus less likely to suffer economic loss because of them. Further, Lui et al also suggest expressing the toxins in plants (column 7, lines 32-38).

Response to Arguments

Applicant urges that the rejection is traversed for the reasons of record (response pg 5).

This is not found persuasive. The rejections are maintained for the reasons of record.

Applicant urges that Lui and Ben-Dov analyzed strains using probes specific to known cry genes but this method requires the presence of sequences with high homology; none of the instant sequences have high homology to known sequences, thus there would be no reasonable expectation of success (response pg 6).

This is not found persuasive because one of skill in the art, using a combination of restriction mapping of the 68 MDa plasmid and probes made from the sequences of proteins from toxin crystals present in HD536, methods taught by Lui l and Ben-Dov, would have a reasonable expectation of success of isolating all the toxin genes on the 68 Mda plasmid; these would include the instant SEQ ID NO:1, 3 and 5. The use of probes specific to known cry genes is not required.

Applicant urges that Lui could not isolate genes using this method and had to partially sequence protein bands fractionated from these isolates, a method by which one of skill in the art can isolate highly expressed sequences; however, lower-expressed genes may be "masked" and Lui provide no guidance for isolating the instant sequences (response pg 6).

This is not found persuasive because Applicant has provided no evidence that SEQ ID NO:1 is a lower-expressed gene. Further, restriction mapping of the 68 MDa plasmid in HD536 and subsequent sequencing of the fragments, would result in isolation of SEQ ID NO:1, 3 and 5. Thus, there was a reasonable expectation of success of identifying the specific genes claimed in the instant application.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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May 10, 2011

/Anne R Kubelik/
Primary Examiner, Art Unit 1638